REMARKS

I. Preliminary Remarks

The Examiner stated the title of the invention is not descriptive. In the foregoing amendment a new title is submitted.

In the foregoing amendment claims 2, 3, 5-25, 28, 33, 35-38 and 40-56 were canceled without prejudice as being directed to unelected subject matter. Applicants reserve the right to pursue these claims or claims of similar scope in continuing applications. Withdrawn claims are directed to methods that may be rejoined when the pending product claims are found to be in condition for allowance.

Amended claim 4 is now directed to the amino acid sequence of SEQ ID NO: 10 and active fragments thereof. Active fragments are supported at page 4, lines 11-16. Fragments and polypeptide variants that bind to a CD8 protein are supported at page 4, line 14-15. In addition, the term "CD8-trophic" refers to a HIV-1 strain that infects CD8 positive cells using CD8 protein as a receptor. (See page 3, lines 11-14). New claim 57 is directed to polypeptides encoded by the nucleotide sequence of SEQ ID NO: 9 under stringent hybridization conditions. The stringent hybridization conditions are defined in the specification at page 7, lines 3-24. New claim 59 is directed to polypeptides having conservative substitutions, which are supported at page 5, lines 3-20. Thus, the amendments to the claims do not add new matter to the application.

II. The rejection under 35 U.S.C. §112, second paragraph should be withdrawn.

Claims 1 and 29 were rejected under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter of the invention. In particular, the Examiner stated that the recitation "set out in" is unclear. In response, the claims are amended to recite "comprising" a particular sequence identification number.

In addition, the Examiner stated that "polypeptide" recited in claim 29 should be plural. Claim 29 has been amended to recite "a polypeptide of any one of claims 4, 57, 58 or 59." The rejections under 35 U.S.C. §112, second paragraph are now moot in view of the foregoing amendment, and Applicants request that these rejection be withdrawn.

III. The rejection under 35 U.S.C. §112, first paragraph should be withdrawn.

Claims 1, 4, 29 and 39 were rejected under 35 U.S.C. §112, first paragraph as the specification does not enable one of skill in the art to make and/or use the claimed invention. Applying the factors set out in *In Re Wands*, 858 F.2d 731, 737, 8 USPQ 2d 1400, 1404 (Fed. Circ, 1988), the Examiner stated that the state of the prior art indicates that one would not expect HIV-1 gp120 to be trophic for CD8, and the specification does not provide any evidence to indicates the regions or mutations taught in the specification are required for CD8 tropism. Applicants traverse this rejection.

The presence of working examples is one of the factors set out in *In Re Wands, id.* that should be considered in determining if the specification enables the pending claims. Examples 1 and 6 describe the isolation of CD8-trophic strains of HIV-1. The experiments described in Examples 2-4 and 8 (pages 14-17 and 23-24) provide evidence that these HIV-1 strains are CD8-trophic by demonstrating that these viruses could infect CD8 positive/CD4 negative cells and these viruses could infect wild type CD8 negative cells, Hela and COS cells, transfected to express CD8. In addition, CD8 blocking antibodies inhibited replication of the CD8-trophic strains and induced syncitia in CD8 positive cells. Thus, the specification provides experimental evidence that CD8 trophic HIV strains do exist and provide guidance on how to identity and use these strains.

The pending claims are directed to gp120 envelope polypeptides of CD8 trophic strains of HIV-1. The specification provides working examples on how to isolate gp120 polypeptides of a CD8 trophic HIV1 virus. In addition, the specification provides various regions that are altered in the CD8 trophic envelope proteins as compared to proteins isolated from CD4 positive cells. For example, the specification teaches changes within the V1, V2, C2 and V4 loops of the gp120 protein of the CD8 trophic HIV-1 strains. The comparison was completed with 7 CD-8 trophic viruses and the Los Alamos Database. This database contains all of the HIV related sequences published in GenBank (See Appendix A). A recent search of Genbank for protein sequence relating to HIV-1 and gp120 identified 13808 entries (See Appendix B). Therefore, Applicants analyzed a large database to identify the changes set out in Example 10.

The Examiner states "there is no evidence of record to indicate that any such correlation [such as those changes set out in Example 10] demonstrates causality, i.e., CD8

trophism." The Examiner has the burden to establish a reasonable basis to question enablement (*In re Wright*, 999 F.2d 1557, 1562, 27 USPQ 2d 1510 (Fed Cir. 1993); MPEP § 2164.04). The examiner does not provide any evidence, other than a statement pointing out the lack of working examples testing each of the identified changes, to questions whether the specification enables the changes within the amino acid sequences of the gp120 envelope polypeptides confer CD8 trophism in the isolated CD8-trophic HIV2 strains.

Amended claim 4 and new claim 59 are directed to the polypeptide comprising the amino acid sequence of SEQ ID NO: 10, variants having conservative substitutions and fragments thereof that bind to a CD8 protein. New claim 57 is directed to a polypeptide encoded by a hybridization variant of SEQ ID NO: 9. The variants and fragments encompassed by the pending claims must be CD8 trophic envelope proteins, meaning these proteins must play a role in the infection of CD8 positive cells. Primarily, one of skill in the art would expect the gp120 envelope proteins and fragments thereof of the invention to bind to CD8 receptor in order to confer infection of the CD8 positive cell. As discussed above, the specification provides working examples to determine whether the variant protein or fragments thereof, when expressed in a HIV1 strain will induce infection of a CD8 positive cell. In addition, the specification teaches amino acid changes there confer CD8-trophism; and therefore, one of skill in the art will understand which changes within the claimed variant gp120 polypeptides will allow the polypeptide to retain the ability to bind to a CD8 protein. Thus, amended claim 4 and new claims 57-59 are enabled by the specification.

The Examiner also stated that there is no guidance in the specification concerning a pharmaceutical composition comprising the polypeptides of the invention. Applicants traverse this statement. The specification enables the polypeptides of the invention, as discussed above, and provides active ingredients for making the claimed pharmaceutical compositions (See page 10, lines 3-16). Dosages and methods of administration of the compositions are standard in the art and would be understood by one of skill in the art. Thus, the specification enables pharmaceutical compositions comprising the polypeptides of the invention.

In view of the foregoing amendment and remarks, claims 4, 29, 39 and 57-59 are enabled by the specification. Therefore, Applicants request that the rejection of claims 4, 29 and 39 under 35 U.S.C. §112, first paragraph be withdrawn.

CONCLUSION

In view of the above amendment and remarks, claims 4, 29, 39 and 57-59 are in condition for allowance, and Applicants request notification of the same.

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Respectfully submitted,

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